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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
WESSENDORF, T	

ART UNIT	PAPER NUMBER
1618	

DATE MAILED: 05/12/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/491,888	Applicant(s) Rigler et al
	Examiner T. Wessendorf	Group Art Unit 1618

☒ Responsive to communication(s) filed on *Apr 12, 1999* .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *107-147* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *107-147* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

1. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 107-147 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

4. A). The recited 'measuring volume is arranged at a distance of < 1000um from a laser focusing optic' is not supported in the as-filed specification. Cf. With original claim 14 which recites for a volume compartment, not a measuring volume.

B). The specification fails to describe a method by which a molecule can be assayed by the laser excited fluorescence correlation spectroscopy(FCS). The specification further fails to teach the different kinds of substituent attached to a molecule such that said substituent fluoresces when exposed to a laser and/or the different material-specific parameters that the molecules possess. The claims cover numerous unspecified parameters for one skilled in the art to determine. The recited molecule would read on a limitless number of compounds, in a modified or unmodified form, that can contain numerous substituent bound thereto. The kind, amount of

molecules present in a sample, the incalculable number of substituents that can be coupled to the molecule, the material-specific parameters that a specific molecule can possess to enable its differentiation and assaying from the numerous molecules contain in a sample are not adequately described. The description in the specification, like the claims, is simply recites any kind of molecule. Not a single or particular molecule or substituent coupled thereto has been exemplified. One skilled in the art is faced with too numerous unpredictable factors before one could determine or measure the intended presence of a specific molecule coupled substituent. For example, it is well known that some molecules such as enzymes, carbonic anhydrase, have a propensity to aggregate or precipitate when derivatized with certain fluorescent reagents, some variants that have been constructed are so unstable that the gene product cannot be isolated as a holoprotein. Variants of these enzymes are known to be generally unreactive under the certain reagents and conditions due to steric hindrance, or that derivatives with cationic hydrophobic reactive dyes were unstable and precipitated rapidly. At the present state of the art, it is difficult to predict which variants will be stable as fluorescent-labeled apoproteins. Furthermore, the use of fluorescence correlation spectroscopy method has been greatly restricted by experimental difficulties, photochemical instability of the fluorescent materials limits the acceptable exciting intensity and hence, the attainable signal-to-noise ratio for a given dye. (Kask, page 163). Observations seem to be appreciated by applicants at e.g., page 33, paragraph 11 of the instant disclosure. Applicants state that '...when selecting dyes, it is of great importance to select those dyes which have a very low tendency to form triplet states. Each triplet state entered raises the

probability of a chemical reaction, does not provide a signal or provides a signal with undesired wavelength and extends the period until the molecule is ready to be exited into the single state again....' (Emphasis added). Accordingly, determination of these numerous factors can only proceed empirically before a precise measurement of a specific molecule in a sample could be determined or assayed. The spec. does not provide enough guidance, direction or working examples that would aid one skilled in the art to practice the claimed invention.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 107, 109-110 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A). The preamble of claim 107 recites for a method of assaying a molecule(s) in a sample but the method steps recite for determining material-specific parameters of said molecule and not methods by which the molecules in a sample are assayed. There seems to be no correlation between the recited method steps and the preamble. The claim appears to be more for detecting for the presence of a molecule in a sample, rather than assaying. Furthermore, It is not clear, within the claimed context, what constitutes a measuring (measured?) volume within a sample or how said measuring volume is determined in a sample such that said volume can be arranged at

the recited distance from a laser focusing optic. The metes and bounds of the recited material-specific parameters are indefinite and unclear as to the materials that is specific for a molecule.

B). Claim 109 is confusing in the recitation that the concentration of said molecules to be assayed is <1uM. Is the concentration predetermined prior to assaying?

C). Claim 110 is indefinite in the recitation of the different material-specific parameters for said substituent and inconsistent with the base claim recitation for the material-specific parameters being for the molecule, not for the substituent.

D). Claims 11-147 are replete with antecedent basis problems in regard to both terminology and concept. These errors are too numerous to identify. However, a non-exhaustive list is presented below. Applicant is requested to supply antecedent basis for terms and concepts throughout the claims. For example, claim 111, change of coordinates of said measuring volume with times defines an apparent diffusion time of said molecules; claim 112, luminophore-labeled ligand having spectroscopic parameters which are correlated with a property or function; claim 118, measuring takes place within said electric field effecting an electric molecular trap(?); claim 119, complexed ligands; claim 120, free luminophore-labeled ligands; claim 122, first electrophoresis step and transporting said complexes formed into said measuring volume in a second electrophoresis step; claim 144, the products of an in vitro protein biosynthesis. Furthermore, the process steps do not appear to correlate and do not seem to further limit the base claim and broadens the base claim.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 107-147 are rejected under 35 U.S.C. 103 as being obvious over any one of Thompson et al, Sorscher et al , Kask et al, Rigler et al or Meyer in view of the facts well known in the art for reasons advanced at pages 12-14, Office action, 12.23.97.

Applicants admit that Ref. D5, Mayer disclose a working distance of 14000 um with respect to the sample. But argue that one having ordinary skill in the art would not accept this distance as a convenient wording (sic, working) distance. Applicants further argued the surprising advantages of the recited limitations. Applicants' arguments is merely conclusory and not supported by factual evidence, especially in the absence of evidence as to the applicability of said working distance to any kind of molecule. Cf. to the specific molecule of Meyer providing optimum result for a specific molecule. Therefore, it is not seen how said advantage can be applicable to any molecule, absence any evidence to the contrary.

With respect to the other references, it is argued that the limitation in the instant claims to a working distance of the measuring volume arranged at a distance of < 1000um from a laser focusing optic is not taught by References D1-D4 As stated, supra, said limitation is not supported in the specification which recites for a volume compartment i.e., a portion of a device which is not the same as a measuring(?) volume of the sample. Since the specification recites for a

volume compartment hence, the prior art positioning of the different parts of the laser relative to the sample would be within the ordinary skill in the art such that an optimum result is obtained. This is especially true since the results obtained in the prior art i.e., material-specific parameters for the molecules is similarly obtained or defined by the prior art.

[Prosecution is being reopened per applicants' request and arguments of Paper26].

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1618.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. Wessendorf whose telephone number is (703)308-3967.

Tdw

5/12/99

PONNATHAPURA ACHUTAMURTHY
PRIMARY EXAMINER
GROUP 1800